IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	
Osamu JOHDO et al.	:	Atty Docket 2000_0694A
Serial No. 09/555,494	:	Group Art Unit 1656
Filed June 1, 2000	:	Examiner F. Ghashghaee

CRYSTALLINE ANTHRACYCLINE ANTIBIOTIC AND PROCESS FOR PRODUCING THE SAME

PATENT OFFICE FEE TRANSMITTAL FORM

Assistant Commissioner for Patents,
Washington, DC 20231

Sir:

Attached hereto is a check in the amount of $920.00 to cover Patent Office fees relating to filing the following attached papers:

Petition for Extension of Time $920.00

A duplicate copy of this paper is being submitted for use in the Accounting Division, Office of Finance.

The Commissioner is authorized to charge any deficiency or to credit any overpayment associated with this communication to Deposit Account No. 23-0975, with the EXCEPTION of deficiencies in fees for multiple dependent claims in new applications.

Respectfully submitted,

Osamu JOHDO et al.

By Warren Cheek

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February 27, 2002

[Check No. 49033]

2000_0694A

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RESPONSE

Assistant Commissioner for Patents,
Washington, D.C.

Sir:

This is responsive to the Official Action dated August 29, 2001, the time for responding thereto being extended for three months in accordance with a Petition for Extension submitted concurrently herewith.

Favorable reconsideration is respectfully requested in view of the following remarks.

Claims 1-6 are rejected under 35 U.S.C. 102 as being anticipated by Horton et al., and separately, by Smith et al., and separately, by Arcomone et al. These grounds of rejection are respectfully traversed. The rejections appear to be a result of a misunderstanding of the present invention and the prior art.

The objective of the present invention is to provide a crystalline form of daunomycin (or daunorubicin, hereinafter abbreviated as DM) which does not possess the defect of "high hygroscopicity and poor stability" of currently available bulk form of DM, which is "widely used as a chemotherapeutic agent for cancer in clinical application". See the specification, page 1, line 28 to page 2, line 10.

The above-mentioned prior art references, on the other hand, each teach novel anthracycline compounds which are different from DM. These prior art references neither disclose conventional

DM nor teach or suggest providing such a specific crystalline form of DM which has low hygroscopicity and high stability as the claimed invention.

As is seen in the Examples and Fig. 1 of the present specification, there are some known crystalline forms of DM having X-ray powder diffraction data as shown in c), g) and h) of Fig. 1. In contrast, the data shown in b) of Fig. 1 is characteristic of the crystalline DM of the present invention. The Examiner's attention is directed to the fact that the DM of the present invention is achieved by crystalizing DM using the claimed solvent system.

As mentioned in Horton, column 1, lines 7-11:

> This invention relates to a series of compounds showing high antileukemic activity...due to substitution of -OH for the known $-NH_2$ at the 3' position of the hexopyranose sugar, i.e. daunosamine. (emphasis added),

Horton et al. thus only discloses anthracycline compounds, different from DM, having a sugar residue which has, at its 3' -position, -OH as a substitute for $-NH_2$ which originally occupies the 3' -position of sugar residue of DM, i.e., daunosamine. Furthermore, it is seen from a comparison between formula (I) of the present application and the sugar moiety in the formula of Horton et al., column 1, lines 21-35, that the compound to which the present invention relates is quite different from the compounds of Horton et al.

Although the Examiner refers us to working examples 1-5 of Horton et al., these examples naturally teach neither the production of DM nor the crystalline form of DM. Working example 5 of Horton et al. shows X-ray powder diffraction data of 7-O-(2,6-dideoxy-α-L-lyxo-hexopyranosyl)daunomycinone 5 (compound No. 5 of "SCHEME 2" in columns 5 and 6). Even about this compound No. 5 which is different from DM, Horton et al. neither teach nor suggest whether or not those showing said X-ray powder diffraction data have such properties as serve to attain the object of the present invention. Hence, even though Horton et al. simply discloses anthracycline compounds of certain crystalline form, it is still unobvious over Horton et al. that it is possible to obtain DM of a crystalline form having special properties of b) from among those having properties of b), c), g) and h).

Like Horton et al., Smith et al. neither teach nor suggest any specific crystalline form of DM. Although disclosing the "synthesis of adriamycin (I)" (please note that -OH os bonded to the 14-position in formula (I); in DM, the 14-position is occupied by H, not OH), Smith et al. make no mention of DM. Although precursors for the synthesis of adriamycin are mentioned in Examples 1-8 of Smith et al., it would be evident that these are not DM.

In Smith et al., some of the precursors are produced by crystallization. Smith et al., however, neither teach nor suggest that the crystallization of precursors gives a crystalline form having properties which are required of the final product of DM of the present invention.

Arcomone et al. disclose "novel glycoside antibiotic: 4' -epi-6' -hydroxydaunomycin". The antibiotic of Arcomone et al. is an epimer of DM, and is clearly distinguished from DM, as would be understood when the bonding manner of -OH at the 4' - and 6' -positions of sugar residue in formula (I) in column 2 of Arcomone et al. is compared with the bonding manner in formula (I) of the present specification.

Arcomone et al. make no mention of the claimed crystalline form of DM (Example 2).

Since the compounds which are provided by these prior art references are different from the novel crystalline DM according to claim 1, it is evident that these references neither teach nor suggest method claims 2-6 of the present application which use a specific solvent system for the crystallization of DM of claim 1.

Accordingly, reconsideration and allowance are respectfully solicited.

Respectfully submitted,

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